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# PURPURA ASSOCIATED WITH BACILLUS MUCOSUS IN THE BLOOD *

G. C. WEIL AND J. W. MCMEANS

*(From the University of Pittsburgh, Pittsburgh, Pennsylvania.)*

Reports of bacteriemia due to members of the bacillus mucosus group of organisms, in which the diagnosis has been verified by blood-culture during life, are comparatively infrequent in the literature. At autopsy, however, cultures have been reported quite frequently in which the evidence was in favor of such infection. In the case here reported capsulated bacilli were twice recovered from the blood and the urine during life, as well as from the heart's blood, various organs, and urine at autopsy. Our case is also of interest in its clinical course, the development of the blood infection from the urethra and the late onset of the purpura.

The term bacillus mucosus capsulatus employed by Fricke for the group of bacteria here referred to, is the one which we prefer rather than bacillus pneumoniae (Friedländer), since the former is descriptive of one of the characteristics common to all the members of the group, is indicative of no particular disease, and is broad enough to include the many Gram-negative capsulated bacilli which show common biological and cultural characters. There has been and still is confusion in the nomenclature, as shown by the long list of names applied to bacteria, which undoubtedly are members of the mucosus group. The general characteristics of the group are as follows: The bacilli occur as short plump rods, singly or in pairs, often coccoid, while long and even thread-like forms may develop and under certain circumstances fairly long chains occur. No spores are formed. Motility is not observed. Capsules are produced in most media, the addition of serum favoring their development. Growth is luxuriant on all media, aerobic conditions being more favorable than anaerobic. A mucus-like substance is formed in the cultures. Coagulated serum, casein and gelatin are not liquefied. Indol is generally not formed in peptone solution. Fermentation to acid and gas of certain carbohydrates is characteristic of the group, the members differing in the carbohydrates they attack,

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and in the degree of fermentation. Marked tenacity of life is exhibited under ordinary conditions.

Pathogenicity for man and the laboratory animals is somewhat variable, but usually present.

In the classification of the organisms belonging to this group we have found that all the Gram-negative capsulated bacilli, which we have obtained in the laboratory from a variety of sources, come under one or the other of three types, as described by Perkins[1] and others.

This led us to adopt the following practical classification, based on the fermentation of certain carbohydrates: (1) The bacillus lactis aërogenes (Escherich), which possesses the most marked power of fermentation, producing acid and large amounts of gas in dextrose, lactose and saccharose broth. It has been our experience to find this member most frequently. (2) The bacillus acidi lactici (the bacillus duodenale of Ford[2]) possesses in a lesser degree the power of fermentation. It produces acid and gas in dextrose and lactose broth, but fails to attack saccharose. It produces very much less gas than the bacillus lactis aërogenes. (3) The bacillus pneumoniae (Friedländer) ferments dextrose and saccharose to acid and a small amount of gas. In our experience these organisms, when thoroughly studied, produce a late and slight fermentation of lactose. Litmus milk is not coagulated. This micro-organism is found much less frequently than either of the other forms.

The difficulties which have arisen in establishing a classification of the members of the mucosus group can, in a great measure, be traced to incomplete examination, and the failure to recognize the fact that organisms which have the ability to ferment carbohydrates may lose the power in whole or in part through changes in environment or unfavorable conditions (Perkins[3]). The fermentation reactions are no more variable than in the bacillus coli recently isolated from water. In making this classification we would not exclude those indefinite organisms reported in the literature, but we would state that they belong, in all probability, to the degenerated or other types referred to.

As a cause of disease, the capsulated Gram-negative bacilli have been recognized in a great variety of pathological conditions, the discussion of which, at this time, would lead us too far afield and we would rather confine our remarks to those points which chiefly concern the case reported in this paper. However, we would here call attention to the occurrence of Gram-negative capsulated bacilli in conditions involving the respirating tract, accessory sinuses, middle-ear, gastro-intestinal tract and not infrequently the genito-urinary tract.

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[1] *Jour. Infect. Dis.*, 1907, 4, p. 951.

[2] *Stud. Roy. Victoria Hos., Montreal*, 1903, p. 1.

[3] *Jour. Infect. Dis.*, 1907, 4, p. 951.

In reviewing the literature we find that the presence of a definite bacteriemia due to the bacillus mucosus is comparatively rare. Wolff[4] was able to collect from all available literature prior to 1909, 39 cases, the organism recovered being referred to as the bacillus pneumoniae (Friedländer). In 11 of these cases the organism was recovered from blood before death. In the remaining cases, however, he states that the clinical and pathologic picture before death was so definite that they might be classified with the cases of true bacteriemia without comment. Nineteen of the 39 cases had their primary focus in the lung, 17 were of cryptogenic origin, 5 arose in the liver and gall ducts, 5 came from the urogenital tract, 2 from otitis media, and 1 from a phagedenic ulcer. In 13 of the 39 cases, metastases were found in the liver (5 times), in the kidney (4 times), in joints (3 times), in the ear (2 times), in the thigh (1), and in the sternocleidomastoid muscle (1). Two of the above cases recovered.

Hirschbrook and Ziemann[5] report a fatal case in which the bacillus lactis aërogenes was isolated at autopsy from the heart's blood and different viscera. Owing to the clinical manifestations and the recovery of the bacillus typhosus from the stools, this case was first looked on as one of ordinary typhoid fever. Subsequently, however, the symptoms became very acute with the development of purpuric spots and a second examination of stools failed to show presence of the bacillus lactis aërogenes widely disseminated in the body. Diffuse petechial hemorrhages were present. From the results of examination after death it was maintained that the condition was one of the bacillus mucosus capsulatus bacteriemia developing secondarily to typhoid.

Closely associated with the systemic infection by the bacillus mucosus is the development of petechial hemorrhages, not only on the skin surfaces, but also in various viscera, and on the lining membranes of the body cavities. In a review of 10 cases, Abel and Hallwacks[6] showed the frequency of occurrence of hemorrhagic purpura associated with the bacillus mucosus in the blood. From the literature we have found that the petechial hemorrhages seem to arise at the time when the patient is overwhelmed with infection, 5 or 7 days prior to death. These hemorrhages make their appearance as an erythematous rash, later developing a more bluish and finally a deep cyanotic character.

It has not infrequently been found that the bacteriemia due to the bacillus mucosus has originated from the genito-urinary tract. Chiari has reported a case of ascending infection of the genito-urinary tract which at autopsy showed cystitis, prostatic and renal abscesses, endocarditis, infarct of the spleen, and purulent meningitis. Howard[7] has also reported a case of bacteriemia arising from the genito-urinary tract showing chronic cystitis, renal abscess, and peritonitis. It is worthy of note that localized infections simulating chronic gleet may result from an infection by the capsulated Gram-negative bacilli. A case of chronic urethritis reported by Avery,[8] and another with urinary fistula from which

[4] Beiträge zur Pathologie der durch den Bazillus Friedländer erzeugten Sepsis, Dissertation, Leipsic, 1909.

[5] *Cent. f. Bakteriol., orig.*, Abt. 1, 1913, 70, p. 281.

[6] Kolle and Wassermann, *Handb. d. Path. Mikroorg.*, 1913, 6, p. 515.

[7] *Jour. Exper. Med.*, 1899, 4, p. 149.

[8] Standard Methods of Water Analysis, 1912, p. 84.

the organisms isolated had characters of the type of the bacillus lactis aërogenes was reported by White.[9] Bernstein isolated capsulated Gram-negative bacilli from an acute epididymitis, and also from a purulent orchitis. Schenk and Weltman isolated capsulated Gram-negative bacilli from the inflamed fallopian tubes. Allen[10] reported a case of gleet due to the bacillus pneumoniae (Friedländer) which, when treated by autogeneous vaccine, was followed by a satisfactory recovery. As an etiologic factor of inflammatory processes in man we find that the bacillus lactis aërogenes had been most frequently isolated.

Heyse,[11] Wildholz[12] and Schnitzer[13] each reported a case of pneumaturia due to the bacillus lactis aërogenes, while Trumpp[14] found one such infection in 29 cases of cystitis in children. In none of these cases did a generalized infection occur, but the symptoms were at times quite severe.

Recently Leutscher[15] reported 2 cases of the bacillus lactis aërogenes infection of the bladder and commented on the infrequent presence of the organism as a cause of cystitis. His cases are interesting. In the first, a woman developed cystitis during the second month of pregnancy and subsequently infected her husband. Both suffered urethritis and cystitis from which the bacillus lactis aërogenes was isolated.

The case which we desire to report was an Italian of 42 years. He was admitted to the Mercy Hospital, April 1, 1913, under the service of Dr. J. P. Griffith. He complained chiefly of painful, frequent, and difficult urination. He stated that the present illness began Jan. 24, 1913, when he suffered a severe chill as well as some bladder distress. He was treated by a physician, and sounds were passed into the urethra. His chills then became periodic, recurring once or twice a week. The patient always recovered completely from effects of each chill and he was able to go about during the intervals.

The patient was slightly emaciated and rather anemic. Considerable tenderness over the left lobe of prostate with slight enlargement. The passage of sounds showed an obstruction in the posterior urethra.

The patient had had the usual diseases of childhood and recovered without complications. He suffered an attack of malaria at 19 years and an attack of pneumonia at 32 years. He had been married 15 years and migrated to America 5 years ago. He developed gonorrhea 20 years ago, which continued in a chronic state many years. Ten years ago he claimed to have had a condition similar to the present from which he fully recovered.

The circulatory, respiratory, and digestive systems appeared normal. The urine showed the presence of a slight amount of albumen and some leukocytes. Gonococci could not be demonstrated.

*April 3.*—Two hours after first passage of sounds, the patient suffered a severe chill and fever, temperature 105.4 F. The patient remained in bed the following day and appeared quite well. Temperature and pulse normal.

*April 9.*—Eight days after admission the stricture was forcibly dilated under anesthesia, which was followed in a few hours by a severe chill and high fever, 105.6 F. The following day the patient was again sufficiently well to leave his bed.

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[9] *Ibid.*

[10] *Vaccine Therapy,* 1910, p. 127.

[11] *Ztschr. f. klin. Med., Berl.,* 1894, 24, p. 130.

[12] *Cor.-Bl. f. schweiz. Aerzte,* 1901, 21, p. 683.

[13] *Internat. Klin. Rundschau,* 1894, 8, p. 265.

[14] *München. med. Wchnschr.,* 1896, 43, p. 1008.

[15] *Bull. Johns Hopkins Hosp.,* 1911, 22, p. 360.

*April 17.*—Sounds were again passed and the patient again suffered a severe chill, with a fever of 103.4 F., from which he fully recovered on the following day. The urethra at this time was quite patent and permitted the passage of a 28 F. sound. Examination of urine at this time showed a slight amount of albumen with a few leukocytes, while in culture the bacillus lactis aërogenes was isolated.

Following the chill on April 17, the patient recovered except for a general muscular soreness and several painful points, especially about the limbs and shoulders. The patient had been receiving ordinary urinary antiseptics. On May 3 he complained of a burning sensation in the bladder and penis, especially during urination.

*May 15.*—Sounds were again passed into the urethra. No evidence of stricture was found at this time. Shortly following the passage of sounds (37 F.) the patient suffered severe chills and fever of 104.6 F. From this date on the temperature persisted with frequent chills and fever. The patient's general condition was not greatly affected, save for great lassitude.

*May 22.*—Following another chill a blood culture was taken. The bacillus lactis aërogenes was isolated.

Blood examination:

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| Hemoglobin | 70 per cent. | Polynuclears | 87 per cent. |
| Red cells | 4,098,000 | Eosinophils | 1 per cent. |
| Leukocytes | 68,000 | Large lymphocytes | 3 per cent. |
| | | Small lymphocytes | 8 per cent. |
| | | Transitional forms | 1 per cent. |

*May 26.*—Since last passage of sounds the patient had a septic temperature with frequent chills; appetite greatly impaired and evidence of emaciation and anemia appearing; pains in limbs and continuous sharp pain over precordium, but examination of chest and heart showed no lesion.

The high temperature continued, the pulse of good volume, not above 120. The chest wall showed petechial hemorrhages, hip and limbs a mottled erythematous condition.

*May 29.*—Examination of prostate revealed a great tenderness, but only slight enlargement. After thoroughly cleansing urethra, a culture of the bacillus lactis was obtained of the prostatic secretion by massaging the posterior urethra.

*May 30.*—The general condition was quite alarming, with vomiting for past few days.

*May 31.*—The temperature was still very high; intense burning and dryness in the throat. A catheterized specimen of urine gave a pure culture of the bacillus lactis aërogenes. Hemorrhagic spots became darker and more diffuse. There was a slight amount of albumen in urine, but no leukocytes. Red cells, 3,870,000; hemoglobin, 65 per cent; leukocytes, 9,700.

*June 1.*—Blood culture was found to contain the bacillus lactis aërogenes.

*June 6.*—For three days the patient appeared very toxic and although rational, he was very nervous. Pain in the chest was intense and continuous. He was unable to swallow much food but had an intense thirst. His temperature was high, but the pulse was not above 130 per minute; the skin showed a diffuse mottling of petechial hemorrhages considerably darker and more bluish than when first observed.

*June 7.*—Death.

It is evident that we were dealing with an infection due to the bacillus lactis aërogenes. Blood cultures on two different days gave a pure growth of the bacillus lactis aërogenes. The cultures were made in 1 per cent. dextrose serum broth and at the end of 24 hours the blood clot was blown up, floating in the medium with many white vertical, candle-like growths.

Cultures of the bacillus lactis aërogenes were also recovered from the prostatic urethra and the urine. From the bacteriologic evidence the genito-urinary tract appeared to be the point of entrance for the development of the bacteriemia.

*Autopsy twenty-four hours after death (Dr. O. Klotz.)*—The surface of the body rather pale, the face yellowish, the teeth poor, mucous membranes pale. Over the neck, chest, abdomen, thighs and arms was a diffuse purpuric rash, which, for the most, was pinhead in size, but which occasionally showed small hemorrhagic blotches, the largest 1.2 cm. in diameter. The face, hands, and legs below the knees, showed none of these spots. The rash was also seen on the back where postmortem lividity was well developed.

There was a single old adhesion near the apex of the left lung and some diffuse adhesions over the diaphragmatic surface of the right lung. The pericardium contained about 150 c.c. of turbid fluid with many lymph flakes; the surface dull and granular with a single calcareous nodule near the apex of the left lung. The heart weighed 550 G. The right ventricle was large; projecting into its upper part just below the pulmonary valve and lying behind the insertion of the tricuspid valves on the septum was a mass, 4 cm. in diameter, the muscle over it of a yellow necrotic color with hemorrhages; the muscle of the right ventricle otherwise pale and cloudy. The pulmonary and tricuspid valves normal. Throughout the muscle of the left ventricle many yellow spots with hemorrhagic streaks or dots. The papillary muscles showed yellow mottling. The coronary arteries over the surface of the left ventricle very prominent, with definite chains of little nodules in some of them. The mitral valve quite healthy, save for a single, small deposit of recent fibrin. The aortic orifice over half its extent obliterated by a massive thrombotic deposit resting on the heart muscle and the aortic valve in front of the posterior coronary artery filling the corresponding sinus; this mass, which completely obliterated half of each of the adjoining valves at this point, was the size of a small walnut. The vegetation rested on that portion of the heart muscle which was observed to project into the right ventricle. The myocardium just below the aortic ring was much thickened and appeared partly necrotic; in cutting it a small necrotic cavity or abscess was entered; the posterior coronary artery passed over the outside of this mass and was so compressed that its lumen was all but obliterated. When more closely examined, the mass was found to occupy a saccular dilatation of the lower portion of the posterior sinus of Valsalva which projected into the musculature of the septum and posterior parietes so that a protrusion had taken place into the septum and right ventricle.

The base of the aorta quite smooth and elastic, nodular plaques in the thoracic and abdominal portions.

The peritoneum, mesentery, and omentum dotted by small petechial hemorrhages, the majority of which were the size of a pinhead.

The gastric mucosa showed numerous petechial hemorrhages and near the pyloric ring were a number of the marked erosions of the surface.

Here and there in the small and large bowel submucosal hemorrhages were observed, at times 1 cm. in diameter.

Along the upper and anterior border of the spleen, which was large, was a yellow area 2.5 cm. in width, with a dark red center which extended into the organ as an infarct; the spleen substance easily broken, dark in color.

The kidneys large, capsule peeled readily; on the surface many small gray areas about the size of a pinhead; in the left kidney one larger yellow area surrounded by hemorrhagic zone; the cortex and medulla not well defined; the small gray dots observed on the cortex seen as fine gray lines on the cut surface.

The bladder small, walls somewhat thick, the mucous membrane everywhere dotted with bright red hemorrhages, the majority of which were of pinhead size. The prostate not enlarged, but showed some small purulent areas in its substance.

The principle results of the microscopic examination may be summarized by saying that there was a chronic and acute myocarditis and suppurative nephritis.

Culture from the heart blood, from the abscess in heart, from the pericardium, bile, contents of small intestines, and from the bladder, all gave the bacillus mucosus. From the abscess in the heart there was isolated also the micrococcus tetragenus.

*Anatomical Diagnosis.*—The bacillus mucosus capsulatus bacteriemia; infectious purpura; acute vegetative aortic, mitral and mural endocarditis, acute mycotic aneurysm of sinus of Valsalva, stenosis of aortic orifice; acute purulent myocarditis; hypertrophy and dilatation of the heart; acute serofibrinous pericarditis; chronic interstitial myocarditis; petechial hemorrhages of skin, pleura, pericardium, stomach, intestines, peritoneum, pelvis of kidney, ureter, and bladder; acute splenitis; splenic infarct; infarcts and multiple abscesses of kidneys; acute purulent prostatitis.

The organisms isolated from the blood, urine, and prostatic secretion before death and those from the blood and various organs at postmortem were carefully studied. They all showed the following characteristics: They appeared mostly in the form of short plump rods with rounded ends, although in some of the older cultures irregularly sized bacilli were seen forming long and short threads. From the milk agar plates, chains of short capsulated diplobacilli were seen. The bacilli were non-motile, definitely Gram-negative, and did not form spores. Capsules were easily demonstrated from the litmus milk and other media.

In plain broth at the end of twenty-four hours there was a slight cloud, which gradually increased, the broth becoming quite milky in appearance with a heavy white gummy sediment and the development of a thin shiny pellicle especially around the edges, forming a ring on the wall of the test tube. There was no odor.

Plain agar slant showed a shiny, luxuriant, well-defined streak at the end of twenty-four hours. This growth later became heaped up and porcelain-white in color, mucoid, watery, with the growth running down to the bottom. It was very viscous, drawing out in long strings with the platinum needle.

In gelatin stab cultures, the organism grew in a spreading white film on the surface, which did not become heaped up but remained quite flat. Along the line of the stab, fine granules were formed which later ran together and formed a compact streak. After considerable time there appeared fine outgrowths from the stab and the gelatin along the stab became quite cloudy. The gelatin was not liquefied and there was no browning after three months.

On potato slant the growth was shiny, cream colored, sticky and showed much gas production. The growth, after two weeks, became pale yellow.

There was no indol formed after four days in Dunham's peptone solution, tested by Ehrlich's paradimethylamidobenzaldehyde test.

Cultures on litmus milk showed marked acidity in twenty-four hours. On the second day there was firm coagulation with later reduction of the litmus, the clot separating from the clear whey. Capsules easily stained by Welch's method.

Dextrose, lactose, saccharose, mannite, and raffinose broths showed fermentation to acid and much gas in twenty-four hours. At the end of two weeks there was complete decolorization of the fuchsin indicator with absorption of a varying amount of the gas. Dulcite was not attacked. Potato starch broth showed gas production, as did also deep potato starch agar.

On litmus milk agar plates (at the end of twenty-four hours) a spreading watery growth developed which ran down on the cover of the Petri dish. When it was lifted off, long strings of the mucoid growths were formed. At the end of twenty-four hours the medium was pale pink, and in several days the reaction became distinctly alkaline. This reaction was limited to the region of the colonies.

The organism is undoubtedly the bacillus lactis aërogenes of the mucosus group. We were unable to list it under the classification in "Standard Methods for Water Analysis."

## SUMMARY

Clinically, the case was a progressively severe bacteriemia in which cultures of the bacillus lactis aërogenes were obtained during life from the blood, urine and prostatic secretion.

Purpura, although a late manifestation, was the result of this infection.

On account of the systemic reactions after each surgical interference of the urethra, we feel convinced that this was the point of entrance of the infection into the blood-stream.

Probably infection of the genito-urinary tract by bacteria of the mucosus group is more common than realized.